

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No.	:	10/571989	Confirmation No. 5552
Applicant	:	Michael Kalafatis	
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TC/A.U.	:	1651	
Examiner	:	Lora Elizabeth Barnhart	
Title	:	EXOSITE-DIRECTED THROMBIN INHIBITORS	
Docket No.	:	CSU-17999	
Customer No.	:	040854	

Declaration Under 37 C.F.R. §1.132

1. I, Michael Kalafatis, am the sole inventor in the above captioned patent application.
2. In 1983, I received B.S. degrees in both Biochemistry and Human Biology from the University of Paris.
3. In 1984, I received an M.S. degree in Biochemistry from the University of Paris.
4. From 1989 to 1994, I was a post-doctoral fellow in Blood Coagulation Research in the Department of Biochemistry at the University of Vermont.
5. At present, and since 2005, I am a Professor of Chemistry at Cleveland State University.
6. Since 2000, I have been an adjunct staff member of the Department of Molecular Cardiology of the J.J. Jacobs Center for Thrombosis and Vascular Biology of The Lerner Research Institute of the Cleveland Clinic.
7. I have authored or co-authored over eighty (80) articles, many of these directed to blood chemistry. Many of these articles have been published in Blood, a Journal of the American Society of Hematology; and the Journal of Biological Chemistry of the American Society for Biochemistry and Molecular Biology.

8. In the above captioned patent application, evidence of the significance of the claimed peptides is presented. Figure 9B reveals that DYDY is a potent inhibitor of factor V because this peptide impairs cleavage of the factor which is a required step during sequential activation of that factor.

9. Figure 10A of the application demonstrates the improved inhibition resulting from the sulfonated peptides of interest, i.e. DYDYQ-1, DYDYQ-2, and DYDYQ-1,2 as compared to non-sulfonated peptides, i.e. DYDYQ. As shown in Figure 10A, increasing concentrations of these peptides resulted in a decrease in the activity of prothrombinase. This is of great interest. However, it is surprising and unexpected that the sulfonated peptides exhibited even greater inhibitory effects. Moreover, it is particularly surprising and unexpected that the sulfonated peptide exhibiting the greatest inhibitory effect is DYDYQ-1,2.

10. Figure 10B of the application illustrates the surprising and unexpected effects of increasing concentration of the peptide DYDYQ upon the reaction kinetics of blood coagulation. That is, the extent of inhibition is surprising from such relatively low concentrations of the peptide.

11. Similarly, Figure 11A of the application illustrates inhibition by the double sulfonated peptide DYDYQ. Such dramatic reductions are remarkable. Moreover, these inhibitory effects are surprising in view of the relatively low concentrations of DYDYQ that were used.

12. Figure 11B of the application illustrates the surprising and unexpected effect of increasing concentration of the sulfonated peptide DYDYQ. The inhibitory impact of the peptide DYDYQ at such relatively low concentrations is surprising.

13. Figure 12 of the application illustrates clotting time as a function of various peptides according to the present invention. It is surprising and unexpected that these peptides, i.e. DYDYQ, DYDYQ-1,2, DYDYQ-1, and DYDYQ-2, would exhibit such relatively long clotting times. Furthermore, it is remarkable that the peptide DYDYQ-1,2 exhibited the clotting time noted in this figure.

14. Figure 13 of the application illustrates clotting time by various claimed peptides. The data presented in this figure is surprising and unexpected, particularly with regard to the noted clotting times.

15. The data presented in these figures is explained in detail in the present application and particularly on pages 46-49. The figures provide extensive information about the claimed peptides.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date

8/26/09

Michael Kalafatis

